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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/610,215	07/05/2000	Walter Gunzburg	2316.2003-000	4735

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EXAMINER
LAMBERTSON, DAVID A

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/31/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/610,215	Applicant(s) GUNZBURG ET AL.	
	Examiner David A Lambertson	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,18 and 22-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-15 and 22* is/are allowed.

6)☒ Claim(s) *18,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of a reply, filed October 18, 2002 as Paper No. 14, to the previous Office Action. Amendments were made to the claims.

Claims 1-15, 18 and 22-24 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, Paper No. 12, mailed June 15, 2002, that is not addressed in this action has been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for introducing a nucleotide sequence into target cells *in vitro* or *in vivo* for the expression a nucleotide sequence specifically encoding a marker gene, does not reasonably provide enablement for introducing *any* nucleotide sequence into *any* target cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. **This is a new rejection not necessitated by amendment.**

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir.

1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

Nature of the invention. The Nature of the invention is a method of introducing *any* nucleotide sequences into *any* target cells. Since there is no limitation with regards to the nature of the target cells, these cells can be located in a human being, and since the instant specification is primarily concerned with delivery of transgenes to humans as part of gene therapy, the claims read on a method of gene therapy.

Scope of the invention. The scope of the invention is very broad, encompassing a method of introducing any nucleotide sequence into any type of target cells. This includes cells that are located within a human being, thereby reading on a method of gene therapy. Thus the claim is not enabled for the entire scope of the target cells as indicated.

State of the art. The state of the art regarding gene therapy techniques is very underdeveloped and unpredictable, owing to a documented lack of success regarding gene therapy treatments. The major obstacles surrounding the lack of success of gene therapy in general, as well as with regard to retroviral vectors and gene therapy, are clearly indicated in the Office Action mailed on October 2, 2001, and will not be repeated for brevity purposes. As these obstacles have not been overcome in the prior art, the skilled artisan cannot turn to the prior art for guidance in practicing the invention.

Number of working examples and Guidance provided by applicant. The instant specification does not overcome the deficiencies documented in the prior art, and no working

examples are provided concerning the use of the specific retroviral vector of the instant invention in gene therapy protocols. As a result, the skilled artisan cannot turn to the instant specification for guidance in practicing the invention as claimed.

Level of skill in the art. The level of skill in the art is very underdeveloped with regard to the use of retroviral vectors in gene therapy. For example, specific parameters regarding the use of vectors for effective delivery of nucleic acids to target cells during gene therapy and sustained gene expression, as well as an ability to predict and overcome the potential deleterious effects of gene therapy, are unavailable in the art.

Unpredictability of the art. While the specification is enabling for introducing a nucleotide sequence into target cells *in vitro* or for introducing a marker gene into cells *in vivo*, introducing genes for therapeutic purposes is not enabled because of the deficiencies surrounding gene therapy practices (see Verma *et al.*, Nature **389**: 239-242 (1997) for review, cited in the previous Office Action mailed on October 2, 2001, and applied as such). In addition, a review by Anderson (*Nature* **392**: 25-30, 1998; see entire document) focuses on the promise and problems specifically facing human gene therapy using retroviral vectors, pointing out that the "problems that investigators face in developing retroviral vectors that are effective in treating disease are of four main types: obtaining efficient delivery, transducing non-dividing cells, sustaining long-term gene expression, and developing a cost-effective way to manufacture the vector" (page 25, right-hand side, first full paragraph). Furthermore, it has been established that "results of clinical trials have been disappointing" because "[E]ven the most successful trial has fallen short of therapeutic efficacy" (Kmiec, *American Scientist* **87**: 240-247, 1999; see entire document, especially page 240, the center column). In consideration of the highly underdeveloped level of

skill of the skilled artisan and the deficiencies in the prior art and the instant specification with regard to effective gene therapy procedures, the skilled artisan would be forced to practice undue and unpredictable trial and error experimentation when practicing the invention as claimed.

The amount of experimentation required to practice the invention commensurate with the scope of the claims would be undue in light of the *In re* Wands factor analysis provided above and as referenced to the previous Office Action therein. As a result, it is established that the invention is not enabled with regard to the full scope of the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection that is necessitated by amendment.**

Claims 23 and 24 recite the limitation "said one or more sequences" in the first lines of each claim. There is insufficient antecedent basis for this limitation in the claim, and it is still uncertain whether or not the one or more sequences refer to the coding sequences or to the promoter sequences. It appears that the deficiency in the amendment was merely an oversight and that "coding" was inadvertently omitted. Replacing "coding" into "said one or more sequences" would be remedial.

Allowable Subject Matter

Claims 18, 23 and 24 are rejected. Claims 1-15 and 22 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A Lambertson whose telephone number is (703) 308-8365. The examiner can normally be reached on 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson
December 26, 2002

DAVID GUZO
PRIMARY EXAMINER